CASE REPORT

FOUR CASES OF CLASSICAL HIRAYAMA DISEASE WITH DIFFERENT STAGES OF EVOLUTION

Venkatesan Nagarajan¹, Rajesh Venkat I², Mahesh I³, Muthuraj k⁴

HOW TO CITE THIS ARTICLE:

Venkatesan Nagarajan, Rajesh Venkat I, Mahesh I, Muthuraj K. "Four Cases of Classical Hirayama Disease with different Stages of Evolution". Journal of Evolution of Medical and Dental Sciences 2014; Vol. 3, Issue 36, August 18; Page: 9435-9444, DOI: 10.14260/jemds/2014/3217

ABSTRACT: Hirayama disease is characterized by progressive muscle wasting and weakness of the distal upper limb especially small muscles of hand(s) predominantly in young males, followed by spontaneous arrest within several years. It was thought to be due to short dura (compared to bony vertebrae), which detaches from its posterior attachment and compresses the cord during every neck flexion leading to minor ischemic damage to anterior horn cells. During progressive stage of the disease application of a cervical collar to restrict neck flexion may minimize the ischemic insult and arrest progression of the disease. Four young male patients presented with painless unilateral wasting and weakness of hand and forearm without involvement of other limbs. MRI shows focal atrophy of cervical cord and extended flexion study reveals detached posterior dura compressing the cord with an enhancing posterior epidural mass confirming the diagnosis of Hirayama's disease. Nerve conduction studies shows predominant ulnar motor involvement compared to median nerve and electromyography showing denervation of lower cervical segment supplementing the diagnosis. Cervical collar is given to arrest the progression if there is any.

KEYWORDS: Hirayama disease, Oblique amyotrophy, Monomelic Amyotrophy, cold paresis, Benign focal amyotrophy, flexion myelopathy.

INTRODUCTION: Hirayama disease is characterized by progressive muscle wasting and weakness of the distal upper limb especially small muscles of hand(s) predominantly in young males, followed by spontaneous arrest within several years and it was thought to be a form of degenerative anterior horn cell disease¹. With the advent of magnetic resonance imaging (MRI), compressive flattening of the lower cervical cord due to forward displacement of the cervical dural sac during neck flexion in these patients was picked-up.¹ So it was postulated that sustained or repeated neck flexion might cause atrophic changes in the cervical cord which was ultimately proved to be due to ischemic changes of anterior horn cells by post-mortem pathological examination.²

During puberty there is a sudden spurt in growth of bony vertebral column compared to dura in these patients resulting in short length of dura which become tighter on neck flexion and ultimately detached from its loose posterior attachment with pedicle³. During every neck flexion the detached dura crushes the cord and anterior spinal artery against the vertebral body resulting in minor ischemia.⁴ Repeated trauma over the years results in atrophy of anterior horn cells and cord causing muscle weakness and wasting⁵.

CASE REPORT: Between August 2013 and July 2014 we have seen four young males presenting with painless wasting and weakness of small muscles of the hand and forearm in the Neurology out-patient in SRM Medical College Hospital and Research Centre. All of them underwent full neurological

CASE REPORT

evaluation (Table 1), and detailed investigations including MR imaging (Table 2), Nerve conduction study of both upper and lower limbs and Electromyography of upper limbs (Table 3).

All of them are workers between the ages of 16 to 24 and the disease started insidiously, progressed slowly and then stabilized after variable progression. All of them are having unilateral wasting and weakness of forearm and small muscles of the hand confining to C7/8 and T1 dermatome. None of them have either C5/6 myotomal weakness in the affected limb or involvement of other limb or any long tract signs, or sphincter disturbance (Fig 1-4). There is neither history of neck pain or radicular pain nor vertebral tenderness. No family history of neuromuscular diseases, atopy or allergic diseases.

MR imaging was done with contrast both in neutral and neck flexion position in all these cases. All of them exhibit loss of cervical lordosis and cord atrophy at different level (Fig 1-4). However for other MRI criteria each one displayed different findings. Case 1 has very mild detachment of posterior dura and smaller crescent shaped posteriorly enhancing mass without much flow void signals whereas Case 2 and 3 have bigger crescents with flow voids signals which are also seen in axial section of case 3. Case 4 has only long intramedullary lesion without any posterior dural compression of the cord or crescent formation during neck flexion. The spectrum of MRI findings may suggest mild, moderate, severe and eventual mended stages of the disease.

Nerve conduction studies (NCS) of all 4 limbs done using standard protocol. Ulnar compound muscle action potential (CMAP) was low in the affected limb in all of them whereas sensory nerve action potential (SNAP) was normal even in the affected limb. 'F waves' were either absent or hard to obtain in the affected limb in all of them (Table 3).

Muscles sampled in electromyography (EMG) of both upper limbs include deltoid, biceps brachii, brachioradialis (C5/6 myotome), flexor digitorum sublimis, flexor carpi ulnaris and radialis (C7/8 myotome), first dorsal interossei, abductor policis brevis and abductor digiti minimi (C8/T1 myotome) and cervical paraspinal muscles. Denervation potentials specifically confined to C7/8 and T1 myotome of the affected upper limb only (Table 3).

DISCUSSION: In olden days, patients presenting with unilateral wasting and weakness with or without fasciculations were considered as a form of focal motor neuron disease and it is called differently as monomelic amyotrophy or benign focal amyotrophy⁶. In 1959, Hirayama et al first reported 12 patients with a benign sporadic juvenile-onset of unilateral wasting and weakness of hand and forearm muscles with gradual progression initially.⁷ As he was able to prove ischemic pathology the disease is named after him.

All of our patients satisfy the clinical diagnostic criteria for Hirayama's disease⁸ namely 1) symptom onset in late adolescence or young adulthood, 2) motor-only syndrome, 3) motor involvement restricted to the upper extremities, 4) asymmetric muscle changes, 5) a period of clinical progression followed by relative stability, and 6) no alternative explanation for symptoms identified during the evaluation. Only one (case 3) has some sensory disturbance. Such a sensory disturbance has been well documented in literature.¹

Apart from clinical evaluation, MRI of cervical spine is a must to rule out other diagnosis and to prove Hirayama disease. All of our patients satisfy MRI diagnostic criteria (table 2) for Hirayama.⁹

Anterior displacement of posterior dura during neck flexion is considered hallmark of this disease.⁹ All our cases has these findings except case 4 which may indicate it is a long drawn disease

CASE REPORT

process in him though he noted the wasting only for the past 3 years. According to Willeit et al¹⁰ if the disease is more than 10 years the dynamic changes will disappear and only cord atrophy secondary to ischemic insult will remain.

Anterior horn cells are more susceptible to ischemic injury in the spinal cord and the segment most commonly involved is C7/8 and T1 with sparing of others.⁵ This is evident in most of the EMG studies done on Hirayama patients.¹¹ Clinically sparing of brachioradialis muscle (C5/6) leading to characteristic oblique atrophy and EMG studies showing denervation potentials confining to C7/8 and T1 myotome in all our patients supplement the diagnosis.

Only case 1 has spill-over of denervation changes in C5/6 myotome. Ulnar nerve (C8/T1 innervation) is more affected than median nerve. It is evidenced by comparing the ratio of CMAP of ulnar and median¹². Normally the ratio is 0.6 to 1.7 whereas in Hirayama's disease it is always less than 0.6.¹² Even though CMAP is low, ulnar SNAP has not shown such a trend. All our patients exhibited these electrophysiological abnormalities unilaterally whereas in case 3 there is subclinical involvement on the other side also.

By their typical clinical features and MRI characteristics all the four patients are diagnosed to have Hirayama's disease. During progressive stage of the disease application of a cervical collar to restrict neck flexion may minimize the ischemic insult and arrest progression of the disease.¹³

History wise none of our patient has progression but it is difficult to gauge this evolution as the disease process is very slow. As long as the basic pathology of the disease, flexion induced anterior displacement of posterior dura persist there is a chance for progression. So except case 4 all the three are given cervical collar to prevent further damage.

This disease should not be considered benign as it affect the hand function irreversibly in young patients in their productive part of the life and jeopardize the quality for rest of their life.

Wasting occurs late in the disease and it is painless so patient presenting to the physician will also be late for any remedial measures. Only way forward is to identify the biomarker and follow these children during their pubertal growth to prevent this dreaded complication in their juvenile period.

LEARNING POINT:

1. Any young person complains of unilateral wasting and weakness of hands needs a detailed neurological evaluation to rule out Hirayama disease.
2. They should undergo MRI cervical spine both flexion and neutral study with contrast.
3. Any focal cervical cord atrophy seen in routine MRI needs to undergo flexion study.
4. All proven case of progressive Hirayama has to be prescribed cervical collar to arrest the progression.

CASE REPORT

Clinical features	Case1	Case2	Case3	Case4	World literature
Sex	M	M	M	M	M:F =20:1 ¹
Age of presentation	24	18	18	22	Mid teens ¹
Age of onset	22	15	17	19	11-25 (17.6) ¹
Stopped Progression within	2 years	2 years	1 year	1.5 years	73% in 5 years ¹
Laterality	Left hand	Right hand	Left hand	Right hand	Mostly Right hand ¹
Cold paresis	No	Present	No	Present	90% ¹
Oblique atrophy	Present	Present	Present	Present	100% ¹⁴
Poly mini myoclonus	Absent	Present	Absent	Present	91% ¹⁴
DTR RUL	Normal	Absent BJ, SJ	Normal	Absent TJ	Variable ¹
DTR LUL	Absent TJ	Normal	Absent TJ	Normal	
Sensory disturbance	No	No	Sensory loss C7/C8 dermatome	No	Absent ¹

Table 1: Clinical profile of the patients

DTR – Deep tendon reflexes, RUL – Right upper limb, LUL – Left upper limb, BJ – Biceps jerk, SJ – Supinator jerk, TJ – Triceps jerk, C – Cervical.

Clinical features	Case1	Case2	Case3	Case4	Hassan et al ¹²
Neutral position					
Cervical lordosis*	Lost	Lost	Lost	Lost	91%
Asymmetrical cord flattening*	Present C5/C6	Present C5/C6	Present C5/C6	Absent	100%
Localized cord atrophy*	Present C5/6	Present C5/D1	Absent	Present C5/6	82%
Intramedullary Hyperintensities*	Present Speckled - C5	Absent	Absent	Present – Linear - C5/7	18%
Neck Flexion					
Loss of posterior dural attachments*	Present	Present	Present	Absent	90%
Anterior shift of posterior dura*	Present	Present	Present	Absent	90%
Prominent epidural flow void*	Present - mild	Present C4/D1	Present C3/D1	Absent	90%
Post contrast					
Enhancing posterior epidural mass*	Present C5/7	Present C4/D1	Present C3/D1	Absent	100%

Table 2: MRI characteristic of the patients

* MRI Diagnostic criteria for Hirayama⁹

C – Cervical, D - Dorsal

CASE REPORT

Nerve conduction features	Case 1		Case 2		Case 3		Case 4	
	Right	Left	Right	Left	Right	Left	Right	Left
Nerve conduction studies								
Ulnar CMAP	9.46	1.36	7.51	13.21	4.76	11.56	0.17	7.92
Median CMAP	10.08	9.58	13.22	14.73	15.8	21.23	7.14	5.31
Ulnar/ Median CMAP	0.94	0.14	0.57	0.90	0.30	0.55	0.23	1.49
Ulnar SNAP	16.95	37.28	24.07	20.91	24.21	21.63	18.32	18.29
Median SNAP	15.54	37.40	25.0	20.12	23.83	21.34	18.48	18.40
Ulnar/ Median SNAP	1.09	1.00	0.96	1.04	1.02	1.01	0.99	0.99
F wave – Median & Ulnar	Normal	Absent	Absent	Present	Absent ulnar	Normal	Impersistance	Normal
Electro Myography								
C5/ C6 myotome	Normal	Neurogenic	Normal	Normal	Normal	Normal	Normal	Normal
C7/8 & T1 myotome	Normal	Neurogenic	Neurogenic	Normal	Neurogenic	Normal	Neurogenic	Normal
Cervical paraspinal	Normal	Neurogenic C7 & C8	Neurogenic C7 & C8	Normal	Neurogenic C7 & C8	Normal	Neurogenic C7 & C8	Normal

Table 3: Neurophysiological characteristics of the patients

C - Cervical

REFERENCES:

1. Hirayama K. Juvenile Muscular Atrophy of Distal Upper Extremity (Hirayama Disease) Internal Medicine 2000; 39: 283-290.
2. Hirayama K, Tomonaga M, Kitano K, Yamada T, Kojima S, Arai K. Focal cervical poliopathy causing juvenile muscular atrophy of distal upper extremity: A pathological study. J Neurol Neurosurg Psychiatry 1987; 50: 285-90.
3. Kikuchi S, Tashiro K, Kitagawa K, Iwasaki Y, Abe H. A mechanism of juvenile muscular atrophy localized in the hand and forearm (Hirayama's disease): flexion myelopathy with tight dural canal in flexion [in Japanese]. Clin Neurol (Tokyo 1987; 27: 412-419
4. Biondi A, Dormont D, Weitzner I, Bouche P, Chaine P, Bories J. MR imaging of the cervical cord in juvenile amyotrophy of distal upper extremity. AJNR Am J Neuroradiol 1989; 10: 263-268.

CASE REPORT

5. Hirayama K. Non-progressive juvenile spinal muscular atrophy of the distal upper limb (Hirayama's disease In: De Jong JM, editor. Handbook of Clinical Neurology. Vol. 15. Amsterdam: Elsevier; 1991. pp. 107–20.
6. Gourie-Devi M, Nalini A. Long-term follow-up of 44 patients with brachial monomelic amyotrophy. *Acta Neurol Scand* 2003; 107: 215-20.
7. Hirayama K, Toyokura Y, Tsubaki T. Juvenile muscular atrophy of unilateral upper extremity: a new clinical entity. *Psychiatr Neurol Jpn* 61: 2190-2198. 1958
8. Tashiro K, Kikuchi S, Itoyama Y, et al. Nationwide survey of juvenile muscular atrophy of distal upper extremity (Hirayama disease in Japan). *Amyotroph Lateral Scler* 2006; 7: 38–45.
9. Pradhan S, Gupta RK. Magnetic resonance imaging in juvenile asymmetric segmental spinal muscular atrophy. *J Neurol Sci.* 1997; 146: 133–8.
10. Willeit J, Kiechl S, Kiechl-Kohlendorfer U, Golaszewski S, Peer S, Poewe W. Juvenile asymmetric segmental spinal muscular atrophy (Hirayama's disease): three cases without evidence of "flexion myelopathy." *Acta Neurol Scand* 2001; 104: 320 –322.
11. Xiu-ming, Xin-yue and Cheng. Neuroelectrophysiological characteristics of Hirayama disease: report of 14 cases. *Chin Med J* 2012; 125 (14): 2440-2443
12. Lyu RK, Huang YC, Wu YR, Kuo HC, Ro LS, Chen CM, et al. Electrophysiological features of Hirayama disease. *Muscle Nerve* 2011; 44: 185-190.
13. Tokumaru Y, Hirayama K. A cervical collar therapy for nonprogressive juvenile spinal muscular atrophy of the distal upper limb (Hirayama's disease). *Clin Neurol (Tokyo)* 1992; 32: 1102–1106
14. Hassan KM, Sahni H, Jha A. Clinical and radiological profile of Hirayama disease: A flexion myelopathy due to tight cervical dural canal amenable to collar therapy. *Ann Indian Acad Neurol* 2012; 15: 106-12.

CASE REPORT

Fig 1: Case 1 A 16 year old male with 2 year history of left hand weakness. Note down the wasting of (oblique atrophy) left forearm with normal right hand (A) and small muscle wasting and clawing of left hand (B). MRI T2 Sagittal Showing minimal cord atrophy at C6 level with Intramedullary hyperintense signal (C – thin arrow). Flexion MRI T2 Saggital showing posterior dura shifting anteriorly and pressing the spinal cord (D – thick arrow) and T1 Gradient axial image showing cord flattening at C 6 level (E).

Fig. 1: Case 1

Fig. 2: Case 2 A 24 yr old male patient presented with weakness of right hand since 3 years with wasting confine to right forearm mainly ulnar side (A) and small muscle wasting esp thenar and hypothenar muscles of right hand (B). MRI T1 fat saturation sagittal imaging showing localized cord atrophy at C-6-C7 level (C – thin arrow). T1 fat saturation post contrast sagittal imaging showing enhancing posterior epidural component with prominent flow voids from C4 to C7 (D – thick arrow). T1 fat saturation post-contrast axial showing mild cord atrophy at C6 (E).

CASE REPORT

Fig. 2: Case 2

Fig. 3: Case 3 An 18 year old worker presented with 1 year history of weakness of right hand with wasting confined to forearm (A) and small muscles of right hand (B). MRI T1 sagittal post contrast showing posterior enhancing epidural component from C3 to D1 (C – thin arrow) and on flexion T2 sagittal image anterior displacement of dorsal dura seen with posterior enhancing mass with flow voids (D – thick arrow). T1 fat saturation post contrast axial image showing flow voids and prominent posterior epidural space (E).

CASE REPORT

Fig. 3: Case 3

Fig. 4: Case 4 A 22 year old worker presented with 3 year history of weakness followed by wasting of forearm (A) and wasting of small muscle of right hand (B). MRI T2 sagittal is showing cord atrophy with linear intramedullary hyperintense signal at C5-C7 level (C – thin arrow) and T1 gradient axial study showing cord atrophy with abnormal intramedullary signal (D – thick arrow). T1 fat saturation post-contrast axial showing mild cord atrophy with intramedullary hyperintense lesions (E).

CASE REPORT

Fig. 4: Case 4

AUTHORS:

1. Venkatesan Nagarajan
2. Rajesh Venkat I.
3. Mahesh I.
4. Muthuraj k.

PARTICULARS OF CONTRIBUTORS:

1. Associate Professor, Department of Neurology, SRM Medical College Hospital & Research Centre.
2. Post Graduate, Department of Neurology, SRM Medical College Hospital & Research Centre.
3. Assistant Professor, Department of Radiology, SRM Medical College Hospital & Research Centre.
4. Professor and HOD, Department of Neurology, SRM Medical College Hospital & Research Centre.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Venkatesan Nagarajan,
Department of Neurology,
SRM Medical College Hospital
& Research Centre,
Kattankulatur, Kancheepuram-603202,
Tamilnadu.
Email: nagarajanusharani@hotmail.com

Date of Submission: 01/08/2014.
Date of Peer Review: 09/08/2014.
Date of Acceptance: 11/08/2014.
Date of Publishing: 16/08/2014.